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Please amend claim 4 as follows:

4. (Amended) The method of claim ~~59~~ 1 wherein the promoter is the human platelet derived growth factor β chain gene promoter.

Please amend claim 5 as follows:

5. (Amended) The method of claim ~~59~~ 1 wherein the region further comprises DNA encoding a second protein, wherein the DNA encoding the Aβ-containing protein and the DNA encoding the second protein are operative linked such that the region encodes an Aβ-containing fusion protein comprising a fusion of the Aβ-containing protein and the second protein.

Please amend claim 7 as follows:

7. (Amended) The method of claim ~~60~~ 2 wherein the Alzheimer's disease marker is a protein and the observed difference is an increase or decrease in the amount of the protein present in the transgenic mouse to which the compound has been administered, or by cells derived from the transgenic mouse to which the compound has been administered.

Please amend claim 9 as follows:

9. (Amended) The method of claim ~~60~~ 2 wherein the Alzheimer's disease marker is a protein and the observed difference is a reduction or absence of the protein in plaques or neuritic tissue present in the transgenic mouse to which the compound has been administered.

Please amend claim 11 as follows:

11. (Amended) The method of claim ~~60~~ 2 wherein the Alzheimer's disease marker is a protein and the observed difference is an increase or decrease in the enzymatic or biochemical activity of the protein in the transgenic mouse to which the compound has been administered, or by cells derived from the transgenic mouse to which the compound has been administered.

Please amend claim 13 as follows:

16 13. (Amended) The method of claim 2 60 wherein the Alzheimer's disease marker is a nucleic acid encoding a protein and the observed difference is an increase or decrease in the amount of the nucleic acid present in the transgenic mouse to which the compound has been administered, or by cells derived from the transgenic mouse to which the compound has been administered.

Please amend claim 15 as follows:

12 15. (Amended) The method of claim 2 60 wherein the Alzheimer's disease marker is a behavior and the observed difference is a change in the behavior observed in the transgenic mouse to which the compound has been administered.

Please amend claim 17 as follows:

14 17. (Amended) The method of claim 2 60 wherein the Alzheimer's disease marker is a histopathology and the observed difference is a decrease in the extent or severity of the histopathology present in the transgenic mouse to which the compound has been administered.

Please amend claim 19 as follows:

18 19. (Amended) The method of claim 2 60 wherein the Alzheimer's disease marker is cognition and the observed difference is a change in the cognition of the transgenic mouse to which the compound has been administered.

Please amend claim 20 as follows:

19 20. (Amended) The method of claim 2 60 wherein the marker is detected or measured using RT-PCR, RNase protection, Northern analysis, R-dot analysis, ELISA, antibody staining, laser scanning confocal imaging, and immunoelectron micrography.

Please amend claim 22 as follows:

E9 22 (Amended) The method of claim 20 wherein the codon encoding amino acid 717 is mutated to encode an amino acid selected from the group consisting of Ile, Phe, Gly, Tyr, Leu, Ala, Pro, Trp, Met, Ser, Thr, Asn, and Gln.

Please amend claim 24 as follows:

E10 24. (Amended) The method of claim 20 wherein the codon encoding amino acid 670 is mutated to encode an amino acid selected from the group consisting of Asn and Glu, or the codon encoding amino acid 670 is deleted, and/or

wherein the codon encoding amino acid 671 is mutated to encode an amino acid selected from the group consisting of Ile, Leu, Tyr, Lys, Glu, Val, and Ala, or the codon encoding amino acid 671 is deleted.

Please amend claim 26 as follows:

E11 26. (Amended) The method of claim 20 wherein the promoter mediates expression of the construct such that $A\beta_{tot}$ is expressed at a level of at least 30 nanograms per gram of hippocampal or cortical brain tissue of the mouse when it is two to four months old, $A\beta_{1-42}$ is expressed at a level of at least 8.5 nanograms per gram of hippocampal or cortical brain tissue of the mouse when it is two to four months old, APP and APPα combined are expressed at a level of at least 150 picomoles per gram of hippocampal or cortical brain tissue of the mouse when it is two to four months old, APPβ is expressed at a level of at least 40 picomoles per gram of hippocampal or cortical brain tissue of the mouse when it is two to four months old, and/or mRNA encoding the Aβ-containing protein is expressed to a level at least twice that of mRNA encoding the endogenous APP of the transgenic mouse in hippocampal or cortical brain tissue of the mouse when it is two to four months old.

Please amend claim 31 as follows:

31. (Amended) The method of claim ~~59~~ 1 wherein the construct further comprises an effective amount of at least one intron, wherein the effective amount of at least one intron is located in the region of the construct encoding the Aβ-containing protein.

Please cancel claim 33.

Please amend claim 34 as follows:

~~34~~ 35. (Amended) The method of claim ~~62~~ 33 wherein the Alzheimer's disease marker is a protein and the observed difference is an increase or decrease in the amount of the protein present in the transgenic mouse to which the compound has been administered, or in cells derived from the transgenic mouse to which the compound has been administered.

Please amend claim 36 as follows:

~~36~~ 37. (Amended) The method of claim ~~62~~ 33 wherein the Alzheimer's disease marker is a protein and the observed difference is a reduction or absence of the protein in plaques or neuritic tissue present in the transgenic mouse to which the compound has been administered.

Please amend claim 38 as follows:

~~38~~ 39. (Amended) The method of claim ~~62~~ 33 wherein the Alzheimer's disease marker is a protein and the observed difference is an increase or decrease in the enzymatic or biochemical activity of the protein in the transgenic mouse to which the compound has been administered, or in cells derived from the transgenic mouse to which the compound has been administered.

Please amend claim 40 as follows:

~~40~~ 41. (Amended) The method of claim ~~62~~ 33 wherein the Alzheimer's disease marker is a nucleic acid encoding a protein and the observed difference is an increase or decrease in the amount of the nucleic acid present in the transgenic mouse to which the compound has been administered, or in cells derived from the transgenic mouse to which the compound has been administered.

Please amend claim 42 as follows:

43 ~~42~~. (Amended) The method of claim 33 ~~62~~ wherein the Alzheimer's disease marker is a behavior and the observed difference is a change in the behavior observed in the transgenic mouse to which the compound has been administered.

Please amend claim 44 as follows:

45 ~~44~~. (Amended) The method of claim 33 ~~62~~ wherein the Alzheimer's disease marker is a histopathology and the observed difference is a decrease in the extent or severity of the histopathology present in the transgenic mouse to which the compound has been administered.

Please amend claim 47 as follows:

48 ~~47~~. (Amended) The method of claim 33 ~~62~~ wherein the Alzheimer's disease marker is cognition and the observed difference is a change in the cognition of the transgenic mouse to which the compound has been administered.

Please amend claim 48 as follows:

49 ~~48~~. (Amended) The method of claim 33 ~~62~~ wherein the marker is detected or measured using RT-PCR, ELISA, antibody staining, laser scanning confocal imaging, and immunoelectron micrography.

Please amend claim 49 as follows:

50 ~~49~~. (Amended) The method of claim 33 ~~62~~ wherein the codon encoding amino acid 717 is mutated to encode an amino acid selected from the group consisting of Ile, Phe, Gly, Tyr, Leu, Ala, Pro, Tip, Met, Ser, Thr, Asn, and Gln.

Please amend claim 51 as follows:

51. (Amended) The method of claim 62 wherein the codon encoding amino acid 670 is mutated to encode an amino acid selected from the group consisting of Asn and Glu, or the codon encoding amino acid 670 is deleted, and

wherein the codon encoding amino acid 671 is mutated to encode an amino acid selected from the group consisting of Ile, Lys, Glu, Val, and Ala, or the codon encoding amino acid 671 is deleted.

Please amend claim 53 as follows:

53. (Amended) The method of claim 62 wherein the Alzheimer's disease marker is selected from the group consisting of $A\beta_{tot}$, $A\beta_{1-42}$, $A\beta_{N3}(pE)$, $A\beta_{x-42}$, and $A\beta_{Insoluble}$.

Please amend claim 54 as follows:

54. (Amended) The method of claim 62 wherein the construct further comprises an effective amount of at least one intron, wherein the effective amount of at least one intron is located in the region of the construct encoding a human amyloid precursor protein.

Please amend claim 57 as follows:

57. (Amended) The method of claim 59 wherein the Aβ-containing protein consists of all or a contiguous portion of a protein selected from the group consisting of APP770 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, APP751 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, and APP695 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717.

Please amend claim 58 as follows:

58. (Amended) The method of claim 25 wherein the region of the construct encoding a human amyloid precursor protein is selected from the group consisting of APP770 cDNA bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; APP751 cDNA bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; the APP695 cDNA bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; APP695, APP751, or APP770 cDNA truncated at amino acid 671 or 685; APP cDNA truncated to encode amino acids 646 to 770 of APP; a combination cDNA/genomic APP gene construct bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; and a combination cDNA/genomic APP gene construct truncated at amino acid 671 or 685.

Please add the following new claims.

59. A method of selecting a transgenic mouse as a model of Alzheimer's disease, comprising

providing a plurality of transgenic mice, each comprising a nucleic acid construct stably incorporated into the genome, wherein the construct comprises a promoter for expression of the construct in a mammalian cell and a region encoding an Aβ-containing protein, wherein the promoter is operatively linked to the region,

wherein the region comprises DNA encoding the Aβ-containing protein, wherein the Aβ-containing protein consists of all or a contiguous portion of a protein selected from the group consisting of

APP770 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, APP751 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, and APP695 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717; a protein consisting of amino acids 672 to 770 of APP; and a protein consisting of amino acids 672 to 714 of APP;

determining expression levels of APP, APPβ, APPα and/or Aβ in each of the transgenic mice;

identifying a transgenic mouse wherein Aβtot is expressed at a level of at least 30 nanograms per gram of brain tissue of the mouse when it is two to four months old, Aβ1-42 is expressed at a level of at least 8.5 nanograms per gram of brain tissue of the mouse when it is two to four months old, APP and APPα combined are expressed at a level of at least 150 picomoles per gram of brain tissue of the mouse when it is two to four months old, APPβ is expressed at a level of at least 40 picomoles per gram of brain tissue of the mouse when it is two to four months old, and/or mRNA encoding the Aβ-containing protein is expressed to a level at least twice that of mRNA encoding the endogenous APP of the transgenic mouse in brain tissue of the mouse when it is two to four months old;

using an offspring of the identified transgenic mouse as a model of Alzheimer's disease.

60. The method of claim 59, further comprising administering a compound to be tested to the offspring or cells derived therefrom, and

detecting or measuring the Alzheimer's disease marker such that any difference between the marker in the transgenic mouse, or by cells derived from the transgenic mouse rodent, and the marker in a transgenic mouse to which the compound has not been administered, or by cells derived from the transgenic mouse to which the compound has not been administered, is observed,

wherein an observed difference in the marker indicates that the compound has an effect on the marker.

61. The method of claim 59, wherein the Aβ-containing protein consists of all or a contiguous portion of a protein selected from the group consisting of

APP770 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, APP751 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671,

690, 692, and 717, and APP695 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717.

33
~~32~~. A method of selecting a transgenic mouse as a model of Alzheimer's disease, comprising

providing a plurality of transgenic mice, each comprising a nucleic acid construct stably incorporated into the genome, wherein the construct comprises a promoter for expression of the construct in a mammalian cell and a region encoding an Aβ-containing protein, wherein the promoter is operatively linked to the region,

wherein the region comprises DNA encoding the Aβ-containing protein, wherein the Aβ-containing protein consists of all or a contiguous portion of a protein selected from the group consisting of

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APP770 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, APP751 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, and APP695 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, a protein consisting of amino acids 672 to 770 of APP; and a protein consisting of amino acids 672 to 714 of APP;

determining expression levels of Aβ and Congo red staining in the brains of each of the transgenic mice;

identifying a transgenic mouse;

wherein Aβ is expressed at a level of at least 50 ng/g brain tissue in the identified transgenic mouse when the transgenic mouse is three months of age; and

using an offspring of the identical transgenic mouse as a model of Alzheimer's Disease.

34 33
~~33~~. The method of claim ~~32~~, further comprising administering a compound to be tested to the offspring or cells derived therefrom, and

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